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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
12/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/040,244	FORCE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11,20-28 and 30* is/are pending in the application.

4a) Of the above claim(s) *22-28 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11, 20-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 10/03/2007, been entered.

Claims 8-11, 20-28 and 30 are pending.

Claims 8-11 and 20-21 are under consideration in the instant application.

Claims 22-28 and 30 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to nonelected inventions.

Claims 1-7, 12-19, 29 and 31have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 10/03/2007.

The rejections of record can be found in the previous Office Actions, mailed 04/05/2007, 10/21/2005 and 01/25/2005.

3. Claims 8-11 and 20-21 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-11 and 20-21 are indefinite in the recitation of "CD40L enhancer antibody (Alexis)" because its characteristics are not known. The use of "CD40L enhancer antibody (Alexis)" as the sole means of identifying the claimed antibody renders the claim indefinite because "CD40L enhancer antibody (Alexis)" is merely laboratory designations which does not clearly define the claimed product, since different laboratories may use the same laboratory designations to define completely distinct hybridomas / cell lines.

Applicant's arguments, filed 10/03/2007, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant relies upon Exhibit A, which is a copy of a product data sheet from Alexis biochemicals, which describes a CD40L and an Enhancer for Ligands (Product No. ALX-804—034), which increases biological activity of CD40L at least 1000-fold.

Applicant further notes that the enhancer for ligands is a cross-linking CD40L antibody and is the CD40L enahancer antibody referenced in claims 8-11 and 20-21.

Applicant also submits that the CD40L enhancer antibody (Alexis) has been available since the filing of the application.

While the Product Data Sheet (Exhibit A) provided by applicant refers to an Enhancer for Ligands (Product No. ALX-804-034),
the product Data Sheet (Exhibit A) provided by applicant is drawn to ALX-850-075 and not to the Enhancer for Ligands (Product No. ALX-804-034).

Also, the claims (nor the specification as filed) do not provide a sufficient identifying name or characteritistic(s) that sets forth the metes and bounds of the claimed "CD40L enhancer antibody (Alexis)".

Further, it does not appear that applicant has provided a verified statement from a person in a position to corroborate the fact, and should state, that the biological material are the biological materials specifically identified in the application as filed and to explain the modifications.

Applicant is invited to clarify the metes and bounds of the claimed "CD40L enhancer antibody (Alexis)" and to provide the appropriate Deposit Accession Number, if appropriate to obviate this rejection.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

4. Claims 8-11 and 20-21 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Applicant's arguments, filed 10/03/2007, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant asserts that the claimed "CD40L enhancer antibody (Alexis)" is adequately described, as evidenced by Exhibit A;
that the CD40L enhancer antibody (Alexis) is commercially available from Alexis Biochemicals and
that this CD40L enhancer antibody has been available since the filing of the application.

It is noted that the rejection of record is under 35 U.S.C. § 112, first paragraph, enablement for biological materials and not for written description, as asserted by applicant.

According to MPEP 2404.01, it is noted that the Office will accept commercial availability as evidence that a biological material is known and readily available only when the evidence is clear and convincing that the public has access to the material.

See the final rule entitled "Deposit of Biological Materials for Patent Purposes," 54 FR 34864, 34875 (August 22, 1989).

The mere fact that the biological material is commercially available only through the patent holder or the patent holder's agents or assigns shall not, by itself, justify a finding that the necessary material is not readily available, absent reason to believe that access to the biological material would later be improperly restricted.

Also according to MPEP 2404.01, biological materials must be known and readily available to the public. Neither concept alone is sufficient. The fact that applicant and other members of the public were able to obtain the materials in question or that they were well-defined in the literature prior to and after the filing date of the application does not establish the upon issuance of a patent on the instant application that such material would continue to be accessible to the public. Applicant did not make of record any of the facts and circumstances surrounding the access to the biological materials, nor is there any evidence as to the policies regarding the materials if a patent would be granted on the instant application. Further, there are no assurances that those entities in control of the claimed biological materials would allow unlimited access to the biological materials if the instant application would mature into a patent.

Further, it does not appear that applicant has provided a verified statement from a person in a position to corroborate the fact, and should state, that the biological material are the biological materials specifically identified in the application as filed and to explain the modifications.

In the absence of evidence that the CD40L enhancer antibody (Alexis) is readily available to the public and that all restrictions imposed by the owner / depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent,

applicant's arguments have not been found persuasive and the rejection is maintained.

Also, it is noted that identifying characteristics or language for the claimed CD40L enhancer antibody (Alexis) has not been provided in the instant application as well with respect to the enablement requirements for biological materials under 35 USC 112, first paragraph. See MPEP 2400.

The following of record is reiterated for applicant's convenience.

It is apparent that the "CD40L enhancer antibody (Alexis)" is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

5. Claims 8-11 and 20-21 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over de Boer (U.S. Patent No. 5,874,082) (1449; #DR) in view of the well know use of human antibodies in the human diagnostic and therapeutic regimens at the time the invention was made as taught by Tomizuka et al. (PNAS 97: 722-727, 2000) (1449; #UUR) AND/OR Ahuja et al. (U.S. Patent No. 6,482,411) (892; of record) AND/OR Kucherlapati et al. (U.S. Patent No. 6,150,584) (1449; #GR) essentially for the reasons of record.

The teachings of antagonistic anti-CD40 antibodies by de Boer et al. are of record and reiterated herein.

De Boer et al. differ from the claimed invention by the well known construction and use of human antibodies in human diagnostic and therapeutic regimens at the time the invention was made.

De Boer et al. teach both agonistic and antagonistic anti-CD40 antibodies (see entire document). De Boer et al. disclose that all anti-CD40 known in the art have a stimulatory effect on B cells (column 2, paragraph 3) and teach antagonistic anti-CD40 antibodies (see Summary of the Invention, Detailed Description of the Invention and Claims). De Boer et al. teach that recombinant forms of antibodies and antibody fragments as well as pharmaceutical compositions thereof can be used for a variety of procedures (see Detailed Description, particularly columns 5-10). De Boer et al. teach a variety of assays to test anti-CD40 antibodies (e.g. B cell proliferation assay, B cell activation assay, immunoglobulin quantification) (see entire document) and that CD40 epitopes can be identified (see column 7, paragraph 4 - column 8, paragraph 2).

The products of the instant claims and the prior art are defined in terms of certain functional characteristics. Comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons. Given the properties of antagonistic anti-CD40 antibodies, including a number of binding and functional assays taught by de Boer, the claimed binding and functional properties of anti-CD40 antibodies would have intrinsic or expected properties associated with said antagonistic taught by the prior art.

The following references have been added to support the well known construction and use of human antibodies in human diagnostic and therapeutic regimens at the time the invention was made to address the recitation of "human anti-human CD40 antibody".

Tomizuka et al. (PNAS 97: 722-727, 2000) teach the use of double trans-chomosomic mice in the production of human antibodies to antigens of interest for studying in vivo functions and therapeutic products (see entire document, including the Abstract, pages 722-723, 727).

Ahuja et al. (U.S. Patent No. 6,482,411) teach the generation of human antibodies in the generation of therapeutic anti-CD40 antibodies of interest (see entire document, particularly columns 41-45; Anti-CD40 Antibodies From Human Lymphocytes; Transgenic Mice Containing Human Antibody Libraries) as well as humanized antibodies (see columns 45-50; Humanized Anti-CD40 Antibodies).

Kucherlapati et al. (U.S. Patent No. 6,150,584) teach the use of human antibodies derived from immunized xenomice to generate therapeutic antibodies to antigens of interest (see entire document), including the leukocyte marker CD40 (see column 9, paragraph 6).

It would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of the secondary references to advantages of therapeutic antibodies that were fully human which contain immunospecific regions with fully human characteristics such as the convenience of recombinant technology and to avoid undesired immune responses to antigens of interest to CD40 as taught by de Boer et al. to obtain antagonistic human anti-human CD40 antibodies with the properties claimed. Further, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the well known methods of generating human antibodies as taught by Tomizuka et al. (see the Abstract, pages 722-723, 727), Ahuja et al. (see columns 41-45), and Kucherlapati et al. (see entire document, including Background Art on columns 1-2, to take advantages of therapeutic antibodies that were fully human which contain immunospecific regions with fully human characteristics (e.g., convenience of recombinant technology, to avoid undesired immune responses) to antigens of interest, including CD40 with antagonistic properties as taught by de Boer et al. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. Applicant's arguments, filed 10/03/2007, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

With respect to the teachings of antagonistic anti-CD40 antibodies by de Boer et al. (U.S. Patent No. 5,874,082) (1449; #DR), the following is noted.

As pointed out previously, the products of the instant claims and the prior art are defined in terms of certain functional characteristics.

Also, comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons.

Again, applicant's reliance upon the comparison of the prior art antagonistic 5D12 CD40-specific antibody with the instant Example 6, pages 68-70 and Figure 10 of the instant specification is acknowledged.

However these comparisons and results were derived under certain assay conditions.

In contrast to applicant's reliance upon the observations with the 5D12 antibody compared to the disclosed F4-465 and No. 72 antibodies in Example 6 on pages 54-56 of the instant specification;

Example 5 on columns 18-19 of de Boer do teach:

"Very potent inhibition occurred. At concentrations as low as 10 ng/ml each, the three anti-CD40 mAbs 5D12, 3C6 and 3A8 inhibited B cell proliferation completely. Half-maximal inhibition was found at about 1 ng/ml."

Note, too, that the prior art is not limited to the murine 5D12 antibody.

Again, the inhibition taught by the reference does anticipate the claimed limitations as they read on inhibiting B cell proliferation when the concentration of the antibody is in the range of 0.1 µg /ml to 10 µg/ml, as encompassed by the instant claims.

Given the properties of both agonistic and antagonistic anti-CD40 antibodies, including a number of binding and functional assays taught by de Boer, the claimed binding and functional properties of anti-CD40 antibodies would have been intrinsic or expected inherent properties associated with said agonistic and antagonistic taught by the prior art.

Further, applicant failed to rebut prima facie showing anticipation absent objective evidence such as side-by-side testing that would address the thrust of the examiner's rejection and establish the lack of intrinsic or expected properties of antagonistic anti-CD40 antibodies in the prior art rejection.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to provide therapeutic antagonistic anti-CD40 antibodies,

incorporating human anti-CD40 antibodies with an inhibitory efficiency of about 50-90% or greater reduction in B cell proliferation when the concentration of the anti-CD40 antibodies are in the range of 0.01 µg/ml and in the presence of a mixture of human flag-tagged CD40L at 1 ug/ml and CD40L enhancer antibody (Alexis) at 1 µg/ml would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing such antagonistic anti-CD40 antibodies for therapeutic regimens.

Applicant's arguments have not been found to be persuasive.

7. As indicated previously, applicant's amendment, filed 10/03/2007, respectfully request that the following double patenting rejections be held in abeyance until allowable subject matter has been indicated.

It is noted that the double patenting rejections have been updated to the status of related applications and U.S. Patents.

For example, it is noted that previously, a provisional rejection was made over copending application USSN 09/844,684, now U.S. Patent No. 7,063,845.

8. Claims 8-11 and 20-21 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable

over claims 1-30 of U.S. Patent No. 7,063,845 and

over claims 1-9, 17-18 and 20-21 of U.S. Patent No. 7,193,064.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to the same or nearly the same anti-CD40 antibodies. Although the instant claims do not recite specific anti-CD40 cell lines or hybridomas expressing said antibodies, such cell lines expressing antibodies were well known and practiced in the antibody art either in the producing of said antibodies (e.g. monoclonal antibody technology or recombinant antibody technology) at the time the invention was made. The patented claims anticipate or render obvious the instant pending claims.

9. Claims 8-11 and 20-21 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of copending application USSN 11/633,716. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to the same or nearly the same anti-CD40 antibodies. Although the instant claims do not recite cell lines or hybridomas expressing said antibodies, such cell lines expressing antibodies were well known and practiced in the antibody art either in the producing of said antibodies (e.g. monoclonal antibody technology or recombinant antibody technology) at the time the invention was made. Although, the instant claims are drawn to human antibodies and the copending claims do not recite human antibodies per se, it was well practiced and known by the ordinary artisan to employ various antibody forms, including human antibodies in clinical practice. In addition to the interacting with human cell receptors and interactions, human antibodies had the well known advantage of being less immunogenic and of having an increased half-life in human patients.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. No claim allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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